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(71) Applicant (for all designated States except US): COM-
PUMEDICS USA, INC. [US/US]; 7950 University Ave-
nue NE, Fridley, MN 55432 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): FUCHS, Manfred
[DE/DE]; Burgwedeltwiete 16h, 22457 Hamburg (DE).

(74) Agent: KLOS, John, F.; Fulbright & Jaworski L.L.P.,
2100 IDS Center, 80 South Eighth Street, Minneapolis, MN
55402 (US).

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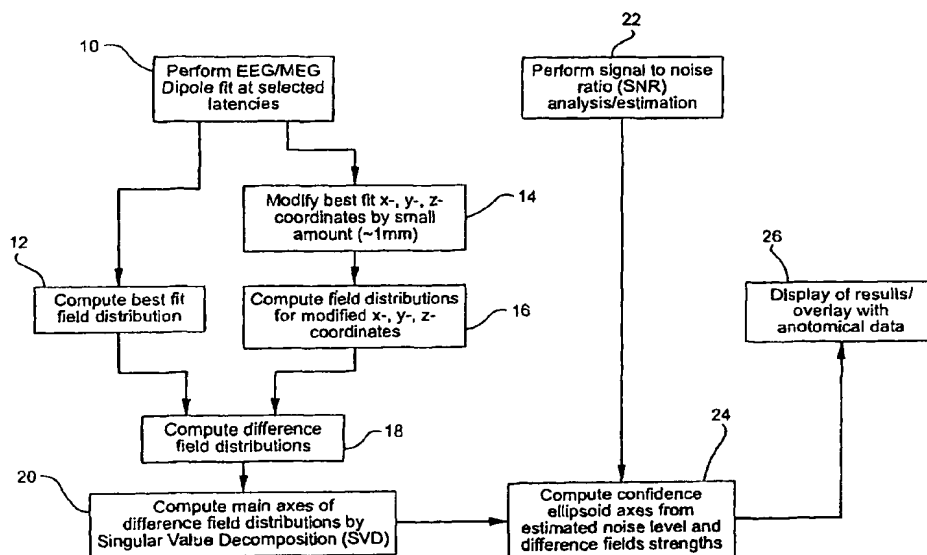
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(54) Title: METHOD AND SYSTEM FOR DISPLAYING CONFIDENCE INTERVALS FOR SOURCE RECONSTRUCTION



(57) **Abstract:** The present invention involves the creation of an appropriate model and the use of that model to generate a best fit dipole represented by a vector (x, y, z). Once the best fit dipole is generated, a best fit field distribution and a field distribution of a modified dipole is created. Using a difference between the field distributions, a Singular Value Decomposition is used to compute the main axes of the confidence ellipsoids.

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(74) Agent: **KLOS, John, F.**; Fulbright & Jaworski L.L.P.,
2100 IDS Center, 80 South Lighth Street, Minneapolis, MN
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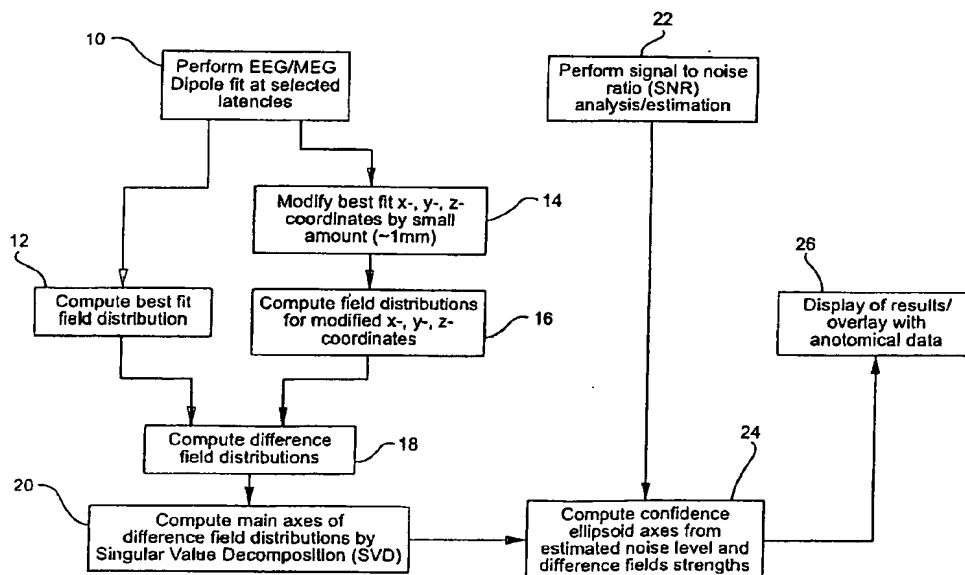
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(72) Inventor; and
(75) Inventor/Applicant (for US only): **FUCHS, Manfred**
[DE/DE]; Burgwedeltwiete 16b, 22457 Hamburg (DE).

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1 Method and System for Displaying Confidence Intervals for
2 Source Reconstruction

3
4 **Field of the Invention**

5 Generally, the invention relates to the field of source imaging. More specifically, the
6 invention relates to the calculation and display of a confidence interval for a dipole fit in a source
7 reconstruction.

8 **Background of the Invention**

9 Physicians and researchers often need to identify patches of electrically active cortical or
10 myocardial tissue in order to identify a source of illness or to map brain activity. While known
11 monitoring equipment are capable of determining that electrical or magnetic activity has occurred,
12 the determination of a source of that activity must often be calculated or estimated. The process of
13 calculating or estimating the source of electro-magnetic activity in tissue is generally referred to as
14 source reconstruction.

15 There are a number of different methods known in the art for performing source
16 reconstruction. Many of these methods involve creating a model which attempts to determine the
17 source of activity through the use of mathematical formulas which describe electro-magnetic field
18 distributions. These formulas typically depend on the position and orientation of the source, the
19 position and orientation of the sensors which pick up the electro-magnetic signals, and the geometry
20 and conductivity properties of the volume conductor (head or chest) tissue.

21 One known method of source reconstruction involves the determination of equivalent current
22 dipoles. This method makes the basic assumption that the source of electro-magnetic activity is
23 focal and small in number. However, measured data exhibits a limited Signal-to-Noise Ratio (SNR)

1 due to background activity, environmental and amplifier noise. The noise distribution of the data
2 leads to scattered dipole positions in the source space around the most probable source position. As
3 such, the reconstructed dipoles only represent the most probable source positions.

4 There is a need for an apparatus and a method to determine and to display an area
5 surrounding the reconstructed dipoles which represent a most probable solution to the source
6 reconstruction model given the noise level in the data. This area is generally known as a confidence
7 interval and it represents a probability distribution which corresponds to the noise level.

8 **Summary of the Invention**

9 The present invention is a method and an apparatus for displaying the confidence interval of
10 a source reconstruction result. In one embodiment, an Equivalent Current Dipole (ECD) model is
11 used to perform the source reconstruction. The ECD model defines a current dipole in terms of its
12 location, strength and orientation, along with an estimate of its reliability (confidence volume).
13 When using the ECD model, one of the vectors generated represents the source dipole location (the
14 more important one since it represents the result of the non-linear least squares fit procedure).
15 Another vector that is reconstructed represents the dipole orientation (solution of a linear inverse
16 problem), so both result vectors should be distinguished. In order to compute the best fit field, both
17 result vectors are needed.

18 Once the best fit dipole is generated, it is used to create a best fit field distribution. The best
19 fit dipole position is also modified by a small amount (generally less than 1mm) and a field
20 distribution of the modified dipole is created. A difference between the best fit field distribution
21 generated and the modified field distribution is computed and a Singular Value Decomposition is
22 used to determine the main axes of confidence ellipsoid. An analysis of the signal noise is
23 performed, and an estimate of the SNR is generated. A confidence interval is calculated from the

1 estimated noise level and the difference of field strength. The confidence interval is then overlaid
2 onto an anatomical image of the source tissue.

3 **Brief Description of the Drawings and Figures**

4 For purposes of facilitating and understanding the subject matter sought to be protected,
5 there is illustrated in the accompanying drawings an embodiment thereof. From an inspection of the
6 drawings, when considered in connection with the following description, the subject matter sought to
7 be protected, its construction and operation, and many of its advantages should be readily understood
8 and appreciated.

9 Fig. 1 is a flow chart of the present invention, the subject method of determining and
10 displaying a confidence interval.

11 Fig. 2 is an illustration of a confidence interval overlaid onto a computer generated image of
12 a cortex.

13 Fig. 3 is an illustration of the confidence ellipsoids as used to test a dipole model used.

14 Fig. 4 is an illustration of a confidence interval overlaid onto an MRI.

15 Fig. 5 is a schematic illustration of the present invention.

16 **Detailed Description of the Preferred Embodiments**

17 A. General Overview

18 Fig. 1 is a flowchart providing a general overview of the present invention. Box 10
19 represents the generation of a dipole fit at selected latencies. This step involves the creation of an
20 appropriate model and the use of that model to generate a best fit dipole represented by a vector (x,
21 y, z). Once the best fit dipole is generated, the vector is used to create a best fit field distribution as

1 shown in box 12. The best fit dipole is also modified by a small amount (generally less than 1mm) as
2 shown in box 14 and a field distribution of the modified dipole is created box 16.

3 A difference between the field distribution generated in box 12 and the modified field
4 distribution of box 16 is computed (box 18). A Singular Value Decomposition is used to compute
5 the main axes of the confidence ellipsoids (box 20).

6 An analysis of the signal noise is performed, and an estimate of the SNR is generated (box
7 22). A confidence ellipsoid is calculated (box 24) from the estimated noise level of box 22 and the
8 difference of field strength from box 20. The confidence interval is then overlaid onto an anatomical
9 image of the source tissue (box 26).

10 B. Operation

11 Reference points are determined with using a Cartesian coordinate system anchored on (at
12 least) three fiducial points on the subject's head. In one embodiment, the fiducial points include two
13 external ear canal points and the nasion. The two ear canal points define the y-axis. The line
14 perpendicular to the y-axis and passing through the nasion defines the x-axis, and the line
15 perpendicular to the x-y plane passing at the intersection of the x-y axis defines the z axis.

16 Once the frame of reference has been established, appropriate models have to be used to
17 reconstruct the source of the measured electro-magnetic data. Neural activity can often be
18 represented as a primary source with a specific current density in a closed volume. The current
19 density is comprised of primary (intracellular) and secondary (extracellular) components.

20 Localizing the primary current sources is known as solving the inverse problem. However,
21 there is typically no unique solution to the inverse problem because there may be an infinite number
22 of current distributions which could be used to explain the externally measured magnetic field or
23 electrical potential. As such, it is necessary to make assumptions regarding the location or the
24 geometry of the source.

1 Given a particular data set, an appropriate model is selected based on a particular model
 2 criterion. There are many model criterion that are known in the art. These formulas depend on the
 3 number, position and orientation of the current source, the position (and orientation in the magnetic
 4 case) of the sensors, and the geometry and conductivity properties of the head or heart tissue. For
 5 the purposes of explanation only, the embodiment of the present invention is described as using an
 6 ECD or elementary dipole model. The ECD model defines the current dipole in terms of its location,
 7 strength and orientation, along with an estimate of its reliability (confidence volume). One skilled in
 8 the art can readily appreciate that the present invention is easily adapted to support other known
 9 models.

10 In order to determine a best fit dipole, the ECD model is used because analytical or
 11 numerical expressions exist that describe their electro-magnetic field distributions. For example,
 12 assuming an infinite homogeneous volume (used for the purpose of simplifying the mathematical
 13 explanation only, typically, spherical shell models, three or four shells representing skin, skull, and
 14 brain, or a Boundary / Finite Element Method model are used) conductor (conductivity σ_0 ,
 15 permeability μ_0) a dipole at position \underline{r}_j , current \underline{j} , sensor at position \underline{r} will have the following electric
 16 potential V_0 and magnetic field B_0 :

$$V_0 = \frac{1}{4\pi\sigma_0} \underline{j} \cdot \frac{\underline{r} - \underline{r}_j}{|\underline{r} - \underline{r}_j|^3} \quad (1)$$

$$\underline{B}_0 = \frac{\mu_0}{4\pi} \underline{j} \times \frac{\underline{r} - \underline{r}_j}{|\underline{r} - \underline{r}_j|^3} \quad (2)$$

17
 18 Due to the linearity in the dipole components of all volume conductor models the so-called
 19 lead-field formulation provides a more compact notation comprising all sensor signals in column
 20 vectors:

$$\underline{V} = \underline{\underline{L}}_V \underline{j} \quad \text{and} \quad \underline{B} = \underline{\underline{L}}_B \underline{j} \quad (3)$$

The lead-field matrices:

$$\underline{\underline{L}}_V (3 \times s_e) \text{ and } \underline{\underline{L}}_B (3 \times s_m)$$

contain all geometric information, such as dipole and sensor positions, and volume conductor properties, whereas the linear dipole components j and thereby the dipole orientations are separated.

In a spatio-temporal formulation, the vector \underline{M} containing the measured data has to be extended to a matrix M , where each column vector represents one sample. Accordingly, the current component vector j has to be extended. For keeping the expressions better readable, the vector and matrix underlines are omitted in the following equations:

$$(j \rightarrow J, \quad \underline{\underline{L}} \rightarrow L, \quad \underline{M} \rightarrow M).$$

The best fit solution of the inverse problem is determined by minimizing the residual variance (squared deviation) between the measured data and the forward calculated fields using the Frobenius norm of a matrix A :

$$|A|^2 = \sum_{i=1}^m \sum_{k=1}^n a_{ik}^2 \quad (4)$$

$$\Delta^2 = |M - LJ|^2 \quad (5)$$

M is the spatio-temporal measured data matrix (s sensors \times t samples), the lead-field matrix L ($s \times c$ current dipole components) comprises the dipole positions, the volume conductor characteristics, and the sensor geometry, and j contains the ($c \times t$) temporal loadings or strengths of the ($c = 3 \times d$ dipoles) dipole components. The best fit currents \hat{j} , that minimize Eq. 5 in the overdetermined case (more knowns than unknowns: $s > c$) are given by [Lawson and Hanson, 1974; Ben-Israel and Greville, 1976]:

$$\hat{j} = (L^T L)^{-1} L^T M \quad (6)$$

The best fit dipole positions can then be found by nonlinear minimization algorithms (e.g. Nelder-Mead-simplex [Nelder and Mead, 1965]) (Box 10). For each dipole position or

1 configuration the lead-field matrix L has to be set up and the best fit deviation (Eq. 5 with $j=\bar{j}$) is
 2 calculated by solving the linear problem for the dipole strengths (Eq. 6). The minimizer changes the
 3 nonlinear parameters (the dipole positions) and looks for the global minimum of the error
 4 hypersurface.

5 Once a best fit coordinate is found, a field distribution is calculated based on the best fit
 6 coordinate (Box 12). The best fit coordinates are also modified (in the order of 1mm) (Box 14) and
 7 a field distribution is calculated based on the modified best fit coordinates (Box 16).

8 From Eq. 5 and 6, the best fit field distribution F is calculated as follows:

$$9 \quad F = L\hat{j} = L(L^T L)^{-1} L^T M \quad (7)$$

10 The difference between best fit field distribution and the modified best fit coordinates is then
 11 calculated (Box 18). By modifying the best fit dipole coordinates $x_i=x, y, z$ by little increments dx_i ,
 12 modified lead field matrices L_i , field distributions F_i , and the difference between the field
 13 distributions dF (normalized to the position changes) corresponding to these changes can be
 14 calculated as:

$$15 \quad dF_i = (F_i - F) / dx_i \quad (8)$$

16 A main axes of the difference in field distributions is then computed by Singular Value
 17 Decomposition (SVD) (box 20). For each dipole position k three difference field vectors dF_k ($i=x, y,$
 18 z) are obtained, that can be written as columns of a difference field matrix dF_k (three columns, s
 19 rows). In a linear approximation, the main axes of the corresponding error ellipsoid can then be
 20 computed by a SVD of this matrix:

$$21 \quad dF_k = U_k \Sigma_k V_k^T \quad (9)$$

22 The axis orientations are contained in rows of the three by three rotation matrix V_k^T and the
 23 lengths of the axes Σ_{ki} are obtained from the number of sensors s (due the normalization of the SVD),

1 the mean noise level N , and the three singular values Σ_{ki}

$$2 \quad l_{ki} = N \sqrt{s} / \Sigma_{ki} \quad (10)$$

3 In this linear approximation the lengths of the confidence ellipsoid axes are proportional to the
4 noise level (Eq. 10) and thus the confidence volume v_k proportional to the third power of the noise
5 level N :

$$6 \quad v_k = l_{kx} l_{ky} l_{kz} \cdot 4\pi / 3 = 4\pi N^3 s^{3/2} / (3 \Sigma_{kx} \Sigma_{ky} \Sigma_{kz}) \quad (11)$$

7 The confidence interval is then overlaid onto an anatomical map, using the coordinates of the
8 best dipole fit and their circumference as shown in Fig. 2. In one embodiment, after registration of
9 the two modalities (functional [EEG/MEG] and anatomical [MR/CT] coordinate system) which is
10 done by matching at least three landmarks that can be identified in both modalities, the confidence
11 ellipsoids can be transformed into the anatomical coordinate system like the dipole positions and
12 orientations using the same transformation algorithm (vector - matrix multiplication representing a
13 rigid transformation [rotation and shift operation]).

14 Fig. 3 is an illustration for the ability of the confidence ellipsoids to be useful to test the
15 dipole model used. In this case a two dipole model was applied to a data-set that could already be
16 explained by a single dipole at the selected latency (Fig. 2). The meaningful dipole stays at the left
17 temporal lobe, whereas the second dipole, that is not really needed to explain the measured data, can
18 be everywhere within the left temporal frontal region. Without displaying the confidence ellipsoids,
19 just two dipole symbols would be displayed, only the fit quality is slightly improved, due to larger
20 degrees of freedom of the two dipole solution (six non-linear (position) parameters and six linear
21 component parameters compared to three non-linear and three linear parameters in the one dipole
22 case). The point cloud in both Fig. 2 and Fig. 3 is the same (points on the segmented cortical surface
23 just for visualization purposes, this could also be a semi-transparent rendering of the cortical
24 surface).

1 As shown in Fig. 4, the confidence ellipsoid can also be overlaid over anatomical data in an
2 orthogonal slice display. The ellipsoids are projected onto the corresponding planes of the
3 anatomical data.

4 5 C. System Configuration

6 As shown in Fig. 5, in one embodiment, the present invention includes a processor 50 in
7 communication with a detector 52, an imaging source 54, and a display 56. For the purposes of this
8 disclosure, the term in communication shall include communication by hardwire means, by
9 telecommunications means, or by the transfer of data using a memory device. The system
10 components can be fully or partially integrated with each other, or they may be stand alone
11 components.

12 The processor 50 can be a single or multiple computers, or can be any processor, integrator,
13 or any hardwired circuit configured to perform the steps described in the subject invention.

14 The detector 52 can be any known physiological monitoring device or a combination thereof.
15 Preferably, the detector is a combination of an Electroencephalogram (EEG) and a
16 Magnetoencephalogram (MEG).

17 The imaging source 54 can be any known imaging device, but preferably, the imaging source
18 is a Magnetic Resonance Imaging Unit (MRI) or a Computerized Tomography Unit (CT).

19 The display can be any that is known in the art, but preferably, the display is of a high
20 resolution.

21 The matter set forth in the foregoing description and accompanying drawings is offered by
22 way of illustration only and not as a limitation. While a particular embodiment has been shown and
23 described, it will be obvious to those skilled in the art that changes and modifications may be made

1 without departing from the broader aspects of applicant's contribution. The actual scope of the
2 protection sought is intended to be defined in the following claims when viewed in their proper
3 perspective based on the prior art.

4

Claims

What is claimed is:

1. A method comprising:

modeling neural activity as a single equivalent current dipole (ECD);

calculating a best fit dipole coordinate;

computing a confidence interval for the dipole coordinate; and

displaying the confidence interval.

2. The method of claim 1, wherein the step of computing a confidence interval includes computing an error ellipsoid.

3. The method of claim 2, wherein the step of computing an error ellipsoid includes computing a main axes of the error ellipsoid using a Singular Value Decomposition.

4. The method of claim 1, wherein the step of modeling includes assuming the geometric and conductive properties of cardiac or cortical tissue.

5. The method of claim 4, wherein the step of computing a confidence interval includes the step determining field distributions for a best fit dipole coordinate and for a modified best fit dipole coordinate.

6. The method of claim 5, wherein the step of computing a confidence interval includes the step of computing the difference field distribution.

7. The method of claim 6, wherein the step of computing a confidence interval includes the step of performing a signal to noise ratio analysis.
8. The method of claim 1, and further comprising defining a Cartesian coordinate system.
9. The method of claim 1, wherein the confidence interval is overlaid on an image obtained through the use of Magnetic Resonance Imaging (MRI).
10. The method of claim 1, wherein the confidence interval is overlaid on an image obtained through the use of Computerized Tomography (CT).
11. An apparatus comprising:
 - a detector;
 - a processor adapted to receive data from the detector, the processor capable of using the data to calculate a best dipole coordinate and a confidence interval; and
 - a display in communication with the processor and adapted to display the confidence interval.
12. The apparatus of claim 11, and further comprising an imaging source in communication with the processor.
13. The apparatus of claim 12, wherein the imaging source is an MRI unit.
14. The apparatus of claim 12, wherein the imaging source is a CT scan.
15. The apparatus of claim 12, wherein the detector is an electroencephalogram.
16. The apparatus of claim 12, wherein the detector is a magnetoencephalogram.
17. A method comprising:

measuring an electrical or magnetic signal;

calculating a best fit dipole coordinate for the signal;

computing a confidence interval for the dipole coordinate; and

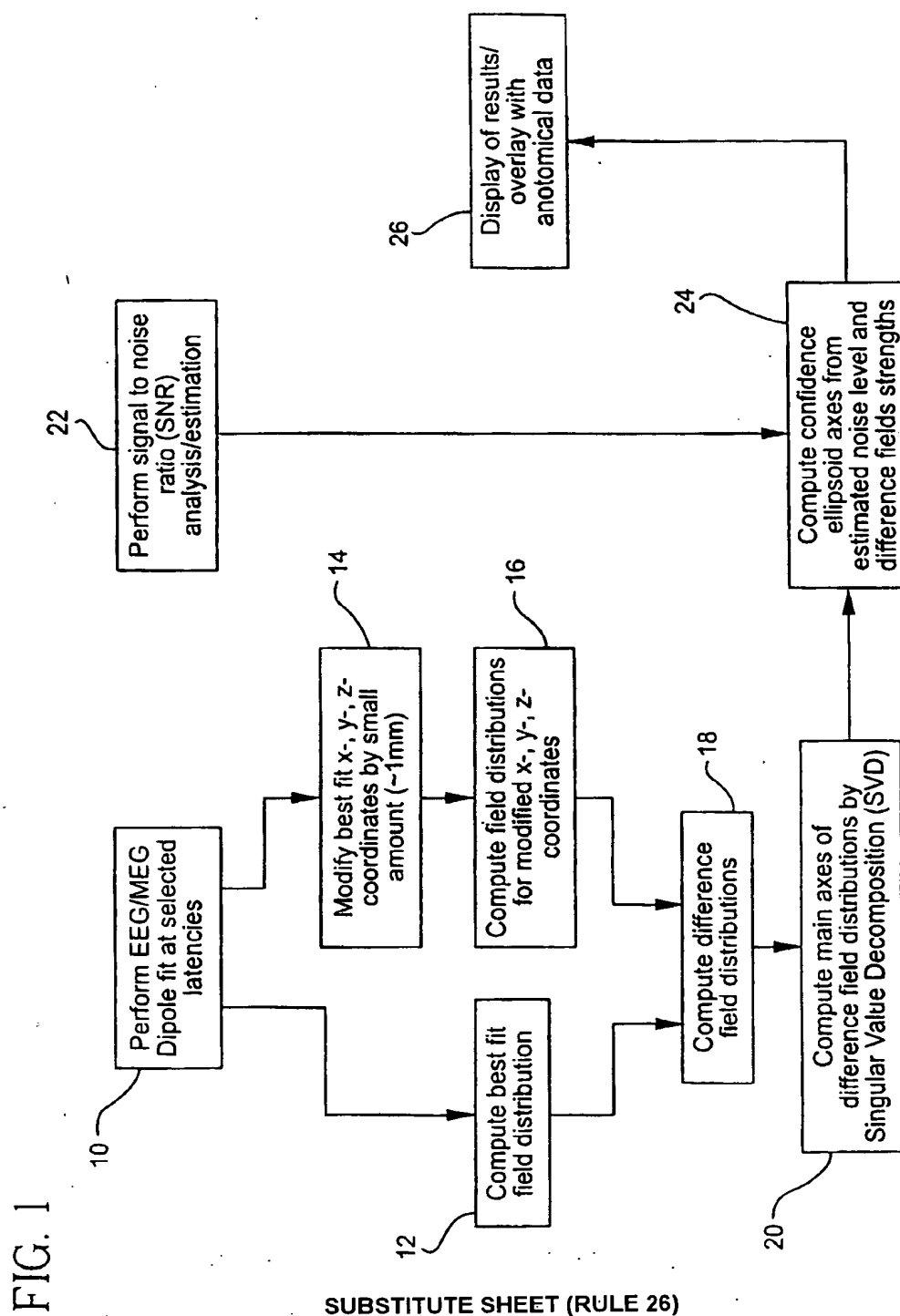
displaying the confidence interval on an anatomical map, wherein the confidence interval is displayed in its anatomical position.

18. The method of claim 17, wherein the step of computing a confidence interval includes computing a confidence ellipsoid axes from estimated noise level and different fields strengths.

19. The method of claim 17, wherein the step of displaying includes the step of receiving a digital image.

20. The method of claim 17, wherein the step of computing a confidence interval includes the step of computing a confidence volume.

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FIG. 2

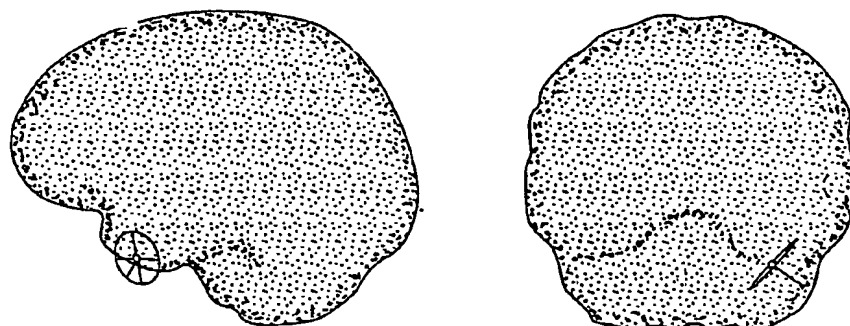
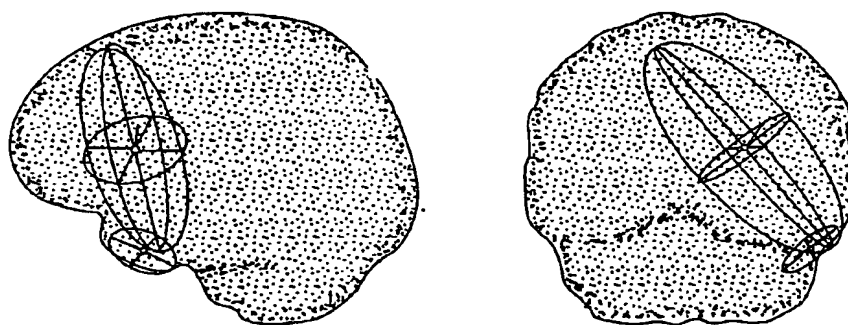
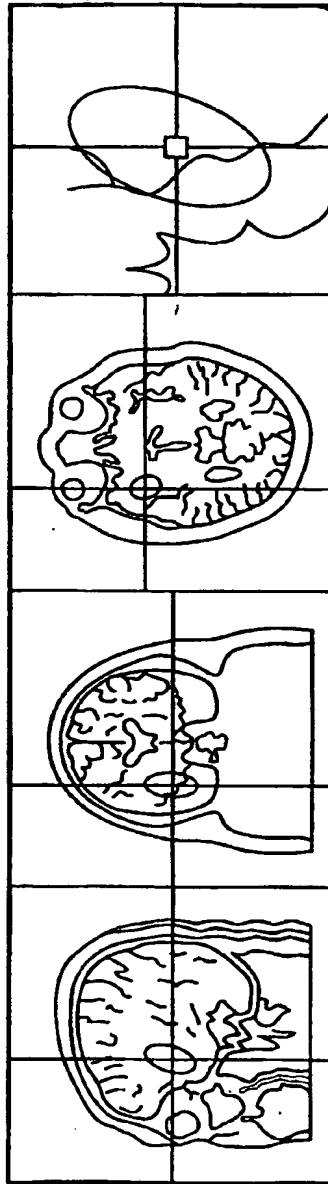


FIG. 3



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FIG. 4



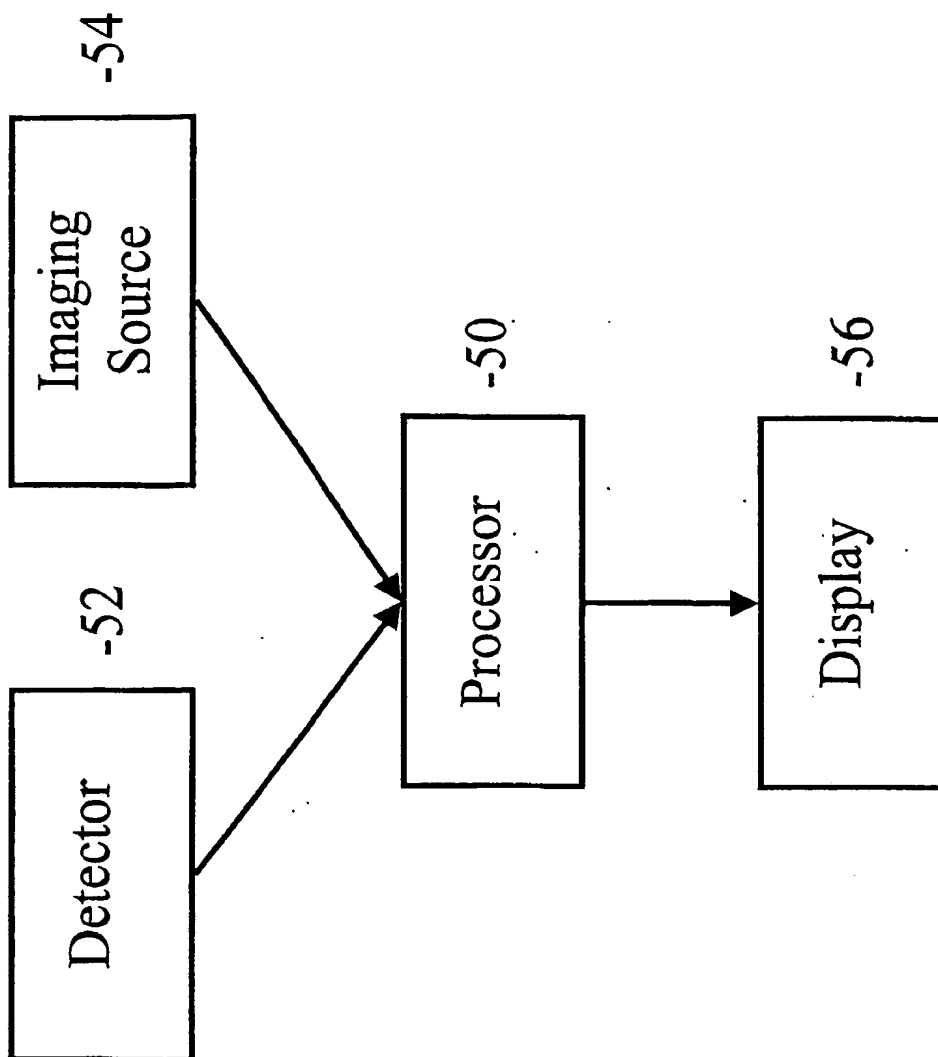


FIG. 5